



Correlation between Parathyroid Hormone Serum Levels and Abdominal Aortic Calcification in Chronic Hemodialysis Patients

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ABSTRACT

Introduction

Abdominal aortic calcification (AAC) significantly contributes to cardiovascular morbidity and mortality in chronic hemodialysis patients. The role of parathyroid hormone (PTH) in this process is complex and intensely debated, with its dysregulation being a central feature of chronic kidney disease-mineral and bone disorder (CKD-MBD). This review synthesizes the literature on the correlation between serum PTH levels and AAC.

Methods

This abstract is based on a literature review synthesizing findings from multiple clinical studies and comprehensive reviews. The review examined the association between PTH levels and AAC, considering the influence of mineral metabolism disturbances, comorbidities, and confounding treatments in chronic hemodialysis patients.

Results

The evidence on the correlation between PTH and AAC is conflicting. Many studies link elevated PTH levels from secondary hyperparathyroidism to increased vascular calcification and cardiovascular mortality. However, this relationship is modified by

other factors, such as patient wasting and the presence of adynamic bone disease. In contrast, a recent study on treatment-naïve patients reported an inverse relationship, where lower PTH levels were associated with higher AAC scores. Other critical risk factors for AAC include diabetes, dialysis duration, and high serum phosphorus levels.

Discussion

The conflicting findings suggest PTH's role in vascular calcification is not linear or isolated. Its effects are likely modulated by the broader state of mineral metabolism, patient nutritional status, and underlying bone turnover. The paradoxical findings in treatment-naïve patients underscore how common therapies, such as calcium and vitamin D supplements, may obscure the natural pathophysiology. This complexity demands a holistic assessment of patient health rather than focusing on PTH levels alone.

Conclusion

The relationship between serum PTH and AAC in hemodialysis patients is complex, with evidence supporting both direct and inverse associations. A comprehensive management approach that considers PTH in the context of calcium, phosphorus, and patient comorbidities is essential to mitigate cardiovascular risk. Further research is needed to clarify these intricate mechanisms.

Keywords

Parathyroid Hormone, Abdominal Aortic Calcification, Chronic Hemodialysis, Mineral Bone Disease, Vascular Calcification.

INTRODUCTION

The correlation between parathyroid hormone (PTH) serum levels and abdominal aortic calcification (AAC) in chronic hemodialysis patients has garnered increasing attention in the literature, particularly in the context of chronic kidney disease (CKD) and its complications. The body of work surrounding this topic reveals a complex interplay between mineral metabolism, vascular health, and patient outcomes.

In their 2008 study, Rodríguez-García et al. highlighted the significance of dialysis duration as a risk factor for vascular calcifications, while noting that high serum hemoglobin levels appeared to mitigate the severity of these calcifications. The authors pointed out a strong association between diabetes and vascular calcifications, particularly in smaller arteries, suggesting that metabolic dysregulation plays a pivotal role in the development of vascular disease among hemodialysis patients. However, the authors also acknowledged the challenges in establishing a clear link between PTH levels and osteoporotic fractures, indicating the need for further exploration of these relationships (Rodríguez-García et al., 2008).

Drechsler et al. (Drechsler et al., 2009) expanded on the complexities of PTH's role in CKD by examining its association with mortality. They found that while elevated PTH levels are often linked to increased cardiovascular events and mortality, the relationship is modified by factors such as muscle wasting, which complicates the interpretation of PTH's effects. This study underscores the necessity of considering various clinical contexts when evaluating PTH's impact on patient outcomes in hemodialysis populations.

The 2011 study by Valson Anna provided a broader epidemiological perspective on mineral bone disease in advanced CKD, discussing how altered mineral metabolism, including PTH levels, contributes to adverse outcomes such as vascular calcification and cardiovascular complications. This comprehensive review pointed out that conventional treatment strategies may not adequately

address low-turnover bone disease, emphasizing the multifaceted nature of bone and mineral disorders in dialysis patients (Valson Anna, 2011).

Cozzolino et al. (Cozzolino et al., 2011) further investigated the implications of secondary hyperparathyroidism (SHPT) in hemodialysis patients, linking elevated PTH levels to cardiovascular morbidity and mortality. Their findings highlighted the critical role of PTH in the pathogenesis of vascular calcification, suggesting that mineral metabolism abnormalities significantly contribute to the high incidence of cardiovascular events in CKD patients. The study also indicated that vitamin D deficiency exacerbates these risks, reinforcing the need for effective management of mineral metabolism in this population.

In a subsequent review, Ivančić (Ivančić, 2011) synthesized current knowledge on the pathogenesis and treatment of SHPT, emphasizing the maladaptive nature of elevated PTH in the context of declining kidney function. The author noted that abnormal mineral metabolism, particularly involving PTH, phosphate, and calcium levels, is linked to increased cardiovascular risk and arterial calcification, thereby underscoring the necessity for targeted interventions in managing these disorders.

Lin et al. (Lin et al., 2011) explored the interplay between serum calcium, phosphorus, and PTH levels in predicting mortality among hemodialysis patients. Their findings indicated that combined serum concentrations of phosphorus and PTH, along with their temporal changes, are significant predictors of adverse outcomes, further elucidating the complex relationship between mineral metabolism and patient survival.

The 2011 investigation by Du et al. (Du et al., 2011) delved into the effects of serum iPTH levels on cardiovascular function in hemodialysis patients. The authors advocated for routine monitoring of iPTH, given its direct correlation with mortality rates. Their results indicated that the management of phosphorus levels is crucial in controlling hyperparathyroidism and, by extension, mitigating cardiovascular risks. Most recently, He et al. (He et al., 2012) specifically examined the association between serum PTH levels and AAC in patients initiating hemodialysis without prior treatment involving calcium or vitamin D analogs. Their findings suggested a counterintuitive relationship, where lower serum PTH levels correlated with higher

AAC scores, challenging the prevailing perceptions of PTH's role in vascular calcification. This study calls for a nuanced understanding of PTH's effects on vascular health, as well as the potential influence of prior treatments on these outcomes.

Together, this body of literature illustrates the intricate relationships between PTH levels, vascular calcification, and patient outcomes in chronic hemodialysis patients, highlighting the need for ongoing research to clarify these associations and inform clinical practice.

LITERATURE REVIEW

The article titled "Vascular calcifications, vertebral fractures and mortality in haemodialysis patients" by (Rodríguez-García et al., 2008) provides a comprehensive examination of the relationship between various clinical and biochemical variables and the prevalence of vascular calcifications in chronic hemodialysis patients. The authors highlight that other meaningful clinical or biochemical variables did not show significant associations with the prevalence and severity of vascular calcifications, emphasizing the complexity of factors influencing vascular health in this patient population.

A notable finding in the article is the association between high serum hemoglobin levels and a lower prevalence of severe vascular calcifications in large and medium caliber arteries. This observation suggests that maintaining adequate hemoglobin levels may play a protective role against vascular calcification, which is a significant concern in hemodialysis patients. Conversely, the authors identify diabetes as a strong risk factor for the prevalence of calcifications, particularly in small caliber arteries, indicating that diabetic patients face a markedly increased risk of vascular calcification, with the risk escalating from 18 to 38 times compared to their non-diabetic counterparts.

The discussion surrounding parathyroid hormone (PTH) levels is particularly pertinent to the topic at hand. While the authors acknowledge that PTH levels might be an independent risk factor for osteoporotic fractures, they also note the challenges in establishing a clear association between PTH and hip fractures in hemodialysis patients, particularly in cross-sectional studies. This aligns with

findings from other studies referenced by the authors, which similarly did not find a significant association between PTH levels and hip fractures in this population. The article titled "The association between parathyroid hormone and mortality in dialysis patients is modified by wasting" by (Drechsler et al., 2009) presents a comprehensive analysis of the relationship between parathyroid hormone (PTH) levels and mortality in patients undergoing chronic hemodialysis, particularly focusing on the role of wasting. The authors effectively highlight the complex interplay between PTH, calcium and phosphate homeostasis, and the implications of these factors in the context of chronic kidney disease (CKD) and end-stage renal disease (ESRD).

A critical evaluation of the material reveals that the authors provide a nuanced understanding of the association between elevated PTH levels and cardiovascular events (CVE) and mortality. They note that while elevated PTH is often linked to increased risks of adverse outcomes in the general population, the situation becomes more convoluted in dialysis patients. The article underscores the variability in findings across different studies, with some indicating a direct correlation between high PTH levels and mortality, while others suggest a paradoxical relationship where low PTH may be associated with worse outcomes ((Drechsler et al., 2009)).

The authors introduce the concept of wasting, a condition characterized by muscle loss and poor nutritional intake, which significantly affects the health of dialysis patients, especially those with diabetes mellitus. They argue that wasting modifies the relationship between PTH levels and adverse outcomes, suggesting that the presence of adynamic bone disease—marked by low PTH levels and reduced bone turnover—could contribute to increased risks of fractures and cardiovascular complications, including aortic calcification ((Drechsler et al., 2009)).

The methodology employed in the study, involving a cohort of 1,255 diabetic hemodialysis patients from the 4D study, adds robustness to their findings. However, while the authors present a compelling argument for the influence of wasting on the PTH-mortality relationship, the article could benefit from a more in-depth exploration of the biological mechanisms underlying these associations.

Additionally, the implications for clinical practice, particularly in managing PTH levels in the context of wasting, could be more explicitly articulated.

The article "Epidemiological profile of mineral bone disease in chronic kidney disease stage 4-5" by (Valson Anna, 2011) provides a comprehensive analysis of the relationship between parathyroid hormone (PTH) serum levels and abdominal aortic calcification (AAC) in patients undergoing chronic hemodialysis. The study highlights the significance of mineral bone disease in the context of chronic kidney disease (CKD), particularly in advanced stages where the regulation of calcium and phosphorus becomes increasingly disrupted.

(Valson Anna, 2011)'s research underscores the pathophysiological mechanisms linking elevated PTH levels with vascular calcification. The article details how hyperparathyroidism, a common complication in CKD, leads to altered calcium and phosphorus metabolism, which in turn contributes to the development of vascular calcification, particularly in the abdominal aorta. The findings suggest that higher serum levels of PTH are associated with increased severity of AAC, indicating a potential biomarker for assessing cardiovascular risk in this patient population.

The methodology employed in the study is noteworthy, as it utilizes a cross-sectional design to evaluate the correlation between PTH levels and AAC in a cohort of chronic hemodialysis patients. However, while the findings are compelling, the article could benefit from a more detailed discussion on the mechanisms underlying the observed correlation. For instance, it would be valuable to explore how other factors, such as inflammation and oxidative stress, may interact with PTH to influence vascular calcification.

Furthermore, the article presents a clear epidemiological profile, yet it lacks longitudinal data that could provide insights into the temporal relationship between PTH levels and the progression of AAC. This limitation raises questions about causality and the potential for therapeutic interventions targeting PTH to mitigate cardiovascular complications in hemodialysis patients.

The article "The Effect of Paricalcitol on Vascular Calcification and Cardiovascular Disease in Uremia: Beyond PTH Control" by (Cozzolino et al., 2011) provides an in-depth examination of the implications of secondary hyperparathyroidism

(SHPT) in patients undergoing hemodialysis (HD) due to stage-V chronic kidney disease (CKD). The authors highlight that SHPT is characterized by elevated serum levels of intact parathyroid hormone (PTH), which is a significant concern for these patients as it is linked to various cardiovascular complications and increased morbidity and mortality.

A critical evaluation of the material reveals that the authors effectively outline the multifaceted relationship between elevated PTH levels, vascular calcification, and cardiovascular health in CKD patients. They emphasize that inadequate management of SHPT can lead to severe health issues, including infections and anemia, which are prevalent among HD patients. This highlights the necessity for healthcare providers to closely monitor and manage PTH levels to mitigate these risks.

The article also discusses the role of vitamin D deficiency in exacerbating vascular calcification, a condition that is notably prevalent in CKD patients. The authors provide a compelling argument that diminished vitamin D levels are significantly associated with an increased risk of vascular calcification, which in turn correlates with higher rates of coronary artery disease and left ventricular hypertrophy (LVH). This connection underscores the importance of vitamin D in maintaining cardiovascular health, particularly in the context of CKD.

Furthermore, the authors delve into the biochemical pathways that link high serum phosphate and calcium-phosphate product levels to cardiovascular events. They argue that these elevated levels contribute to progressive calcium deposition in vascular tissues, leading to detrimental cardiovascular outcomes. The correlation established by Goodman et al. between coronary artery calcification and factors such as dialysis duration, serum phosphorus, and calcium-phosphate product levels reinforces the need for vigilant monitoring of these parameters in HD patients.

The article "Secondary hyperparathyroidism: update on pathogenesis, diagnosis and treatment" by (Ivančić, 2011) provides a comprehensive overview of secondary hyperparathyroidism (SHPT) in the context of chronic kidney disease (CKD) and its implications for vascular calcification, particularly relevant for patients undergoing hemodialysis. The author emphasizes the maladaptive response of

SHPT that arises from declining kidney function, which is a critical aspect in understanding the correlation between parathyroid hormone (PTH) serum levels and abdominal aortic calcification in this patient population.

Ivančić highlights that SHPT is characterized by elevated PTH levels, which, alongside other factors such as phosphate and calcium imbalances, contributes to the pathophysiology of CKD-mineral bone disorder (CKD-MBD). This condition is particularly concerning as it not only affects skeletal health but also has significant implications for cardiovascular health. The article notes that cardiovascular disease is the leading cause of mortality in CKD patients, with those on dialysis facing an extraordinarily higher risk compared to the general population. This stark statistic underscores the necessity of addressing mineral metabolism disorders, as they are implicated in the acceleration of vascular calcification, a process that can lead to increased cardiovascular events.

The review further discusses various treatment strategies, including dietary phosphorus restriction, phosphate binders, vitamin D sterols, and calcimimetics, which are crucial for managing SHPT and potentially mitigating the risks associated with vascular calcification. By controlling PTH levels and other mineral parameters, these interventions aim to improve patient outcomes and reduce the prevalence of cardiovascular complications.

The article titled "Effect Modifying Role of Serum Calcium on Mortality-Predictability of PTH and Alkaline Phosphatase in Hemodialysis Patients: An Investigation Using Data from the Taiwan Renal Registry Data System from 2005 to 2012" by (Lin et al., 2011) presents a comprehensive analysis of the interplay between parathyroid hormone (PTH), serum calcium, and alkaline phosphatase levels in predicting mortality among hemodialysis patients. The study's findings are particularly relevant to understanding the correlation between serum PTH levels and abdominal aortic calcification in chronic hemodialysis patients, as it delves into the broader implications of mineral metabolism disturbances in this population.

The authors systematically evaluate the relationships between serum phosphorus, calcium, and PTH concentrations, emphasizing their significance in the context of cardiovascular morbidity and mortality. The article highlights that elevated PTH

levels are often associated with increased risk of cardiovascular calcification, a common complication in patients undergoing hemodialysis. This correlation is critical, as cardiovascular disease is a leading cause of death in this demographic. By utilizing data from the Taiwan Renal Registry, the authors provide a robust statistical analysis that supports the hypothesis that changes in serum PTH and calcium levels can serve as predictors of mortality risk.

Moreover, the article underscores the importance of correcting serum calcium levels when assessing PTH's predictive capabilities. The authors argue that both uncorrected and albumin-corrected calcium levels should be considered in clinical assessments, as they can significantly influence the interpretation of PTH levels and their associated mortality risk. This point is pivotal for clinicians managing patients with chronic kidney disease, as it suggests that a nuanced understanding of mineral metabolism can lead to better patient outcomes.

The technical characterization of the Bio-PTH (1–84) immunochemiluminometric assay compared to a second-generation assay is another significant contribution of the study. This aspect of the research provides insight into the reliability and accuracy of PTH measurements, which are essential for effective patient management. The authors' exploration of the implications of calcium-containing phosphate binders on cardiovascular calcification further enriches the discussion, linking treatment modalities to patient outcomes.

The article titled "Analysis of the parathyroid function in maintenance hemodialysis patients from Changchun, China" by (Du et al., 2011) provides significant insights into the relationship between parathyroid hormone (PTH) serum levels and various health complications in chronic hemodialysis patients, particularly focusing on secondary hyperparathyroidism. The authors highlight that secondary hyperparathyroidism is a prevalent complication in patients with chronic kidney disease undergoing maintenance hemodialysis, primarily resulting from hypocalcemia and leading to elevated serum intact parathyroid hormone (iPTH) levels.

One of the critical evaluations presented in this article is the dual role of iPTH and calcium in influencing cardiovascular health. The authors assert that while iPTH

has a vasodilatory effect, hypercalcemia is detrimental as it contributes to vascular calcification and left ventricular hypertrophy. This duality underscores the complexity of managing patients with chronic kidney disease, where both low calcium and high phosphorus levels can significantly impact cardiovascular function and overall mortality rates. The article emphasizes the necessity of regular iPTH monitoring, which is crucial for managing secondary hyperparathyroidism effectively and reducing associated risks.

The authors also provide empirical data indicating that serum phosphorus levels were significantly higher in the abnormal group compared to the normal group. This finding reinforces the importance of phosphorus control in managing hyperparathyroidism among hemodialysis patients. The use of phosphate binders as the initial treatment strategy is highlighted, reflecting a clinical approach to mitigate the adverse effects of elevated phosphorus levels.

The article titled "Relationship between serum parathyroid hormone levels and abdominal aortic calcification in patients starting hemodialysis who have never taken calcium tablets, calcitriol, or vitamin D analogs" by (He et al., 2012) provides valuable insights into the complex relationship between serum parathyroid hormone (PTH) levels and abdominal aortic calcification (AAC) in a specific cohort of chronic kidney disease (CKD) patients undergoing hemodialysis.

The authors conducted a thorough investigation into this relationship, focusing on patients who had not previously received treatments that could influence calcium metabolism, thereby allowing for a clearer analysis of the natural correlation between PTH levels and AAC. The study's results indicated that lower serum PTH levels were associated with higher AAC scores in this population, suggesting a potential direct pro-calcification effect of PTH. This finding aligns with the notion that AAC may serve as an independent risk factor for all-cause mortality and cardiovascular disease (CVD) events in various patient populations, including those with CKD ((He et al., 2012)).

Moreover, the article highlights the presence of PTH receptors in myocardial cells, vascular smooth muscle cells, and endothelial cells, which supports the hypothesis that inappropriate secretion of PTH could adversely affect cardiovascular health.

However, the authors also acknowledge the ongoing debate regarding the exact impact of PTH on AAC in CKD patients, referencing previous studies that present conflicting results. Some studies have suggested a correlation between serum PTH levels and the severity of AAC, while others have reported no significant association or even a negative correlation.

This discrepancy may be attributed to the confounding effects of treatments such as calcium tablets and vitamin D analogs, which are commonly used in CKD management and could alter the natural progression of AAC. The authors effectively illustrate the complexity of this issue, emphasizing the need for further research to clarify these relationships and the mechanisms involved.

CONCLUSION

The literature surrounding the correlation between parathyroid hormone (PTH) serum levels and abdominal aortic calcification (AAC) in chronic hemodialysis patients presents a multifaceted view of the interplay between mineral metabolism and vascular health. The introduction highlights the significance of PTH in the context of chronic kidney disease (CKD) and its associated complications, particularly vascular calcifications. (Rodríguez-García et al., 2008) emphasize the role of dialysis duration and metabolic dysregulation, particularly in diabetic patients, as critical factors influencing vascular health. (Drechsler et al., 2009) further complicate the understanding of PTH's effects by linking elevated levels to increased cardiovascular morbidity and mortality, while (Valson Anna, 2011) discusses the broader implications of altered mineral metabolism in advanced CKD. The subsequent studies delve deeper into the relationship between elevated PTH levels and cardiovascular complications. (Cozzolino et al., 2011) assert that secondary hyperparathyroidism (SHPT) significantly contributes to cardiovascular morbidity, while (Ivančić, 2011) provides insights into the maladaptive nature of elevated PTH in declining kidney function. (Lin et al., 2011) and (Du et al., 2011) emphasize the importance of monitoring serum calcium, phosphorus, and PTH levels as predictors of mortality and cardiovascular function.

(He et al., 2012) challenge traditional notions by presenting findings that lower serum PTH levels correlate with higher AAC scores, suggesting a need for a

nuanced understanding of PTH's role in vascular health. This complexity is further reflected in the literature analysis, which highlights various studies that explore the multifactorial nature of vascular calcification, including the effects of serum hemoglobin levels, diabetes, and mineral metabolism disorders.

In conclusion, the body of literature indicates a complex relationship between PTH serum levels and AAC in chronic hemodialysis patients, suggesting that while elevated PTH is often associated with adverse outcomes, the interactions with other clinical factors, such as calcium and phosphorus levels, as well as patient-specific conditions like wasting and diabetes, must be considered. Future research should focus on elucidating these relationships and their implications for clinical practice, particularly in developing targeted interventions for managing mineral metabolism in this vulnerable population.

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